CHAPTER 12

Chest Pain

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Chest pain is one of the cardinal symptoms in medicine. Chest pain is the chief complaint responsible for more than 5.3 million emergency room (ER) visits per year; it accounts for 5% of all ER visits. The challenge to the primary care physician is to differentiate patients who have chest pain as a result of a life-threatening cause from those presenting with chest pain from a benign cause. A thorough history and physical examination are critical in the evaluation of all cases of acute chest pain.

The life-threatening causes of chest pain include acute coronary syndromes, aortic dissection, pulmonary embolus, pneumothorax, and pericarditis with tamponade. Despite our best efforts, up to 8% of patients with chest pain from a life-threatening cause will be incorrectly diagnosed and inappropriately sent home. This chapter focuses on the more common causes of chest pain: acute coronary syndrome, stable angina, aortic dissection, pulmonary embolism, pericarditis, pneumonia, pneumothorax, gastroesophageal reflux, musculoskeletal chest wall pain, and herpes zoster.

ACUTE CORONARY SYNDROME

Acute coronary syndrome (ACS) is the most common life-threatening cause of chest pain. More than 1.4 million patients are admitted annually for ACS.

More than 1 million myocardial infarctions occur each year. ACS includes three distinct conditions: ST-segment elevation syndrome (STEMI), unstable angina (UA), and non–ST-segment elevation myocardial infarction (NSTEMI).

The three acute coronary syndromes are usually the result of the sudden rupture of a *soft* cholesterol-rich coronary artery plaque. This event occurs commonly between 6 AM and noon. The three syndromes are distinguished by the electrocardiographic findings, and cardiac biomarker levels.

Risk factors for ACS include hypertension (blood pressures >140/90 mm Hg), dyslipidemia, diabetes mellitus, smoking, obesity, physical inactivity, family history for premature coronary artery disease (CAD), and metabolic syndrome.

Symptoms

- ACS presents with chest pain *qualitatively* similar to typical angina; however, *quantitatively* it is more frequent, intense, or prolonged than typical angina.
- New onset anginal pain
- Anginal pain at rest or at low effort
- Anginal pain occurring at a decreased effort
- Anginal pain occurring with increased duration (>20 minutes) or intensity despite rest or NTG
- Anginal pain occurring post acute myocardial infarction (MI)
- Atypical anginal pain presenting in a sudden onset or crescendo pattern

Signs

- Few signs with ACS unless there is a sudden decrease in systolic or diastolic left ventricular (LV) function
- Transient hypotension during chest pain +
- Transient cardiac gallops (S_3 or S_4) at the cardiac apex during chest pain ++
- Transient mitral insufficiency secondary to papillary muscle dysfunction during chest pain, associated with a soft S_1 at the left lower sternal border ++

Workup

- ECG
  - Should be measured as soon as possible after presentation with acute chest pain
  - May be normal in up to 20% of patients with ACS and 10% with acute MI ++
  - If ECG is normal, but high clinical suspicion of ischemia is present, ECG should be repeated.
    - Determine *location* of ECG change—Related to coronary anatomy
      - II, III, aVF inferior wall—Right coronary artery (RCA)
      - V1-3 anteroseptal wall—Left anterior descending coronary
      - I, aVL, V4-6 anterolateral wall—Circumflex coronary
      - I, aVL, V1-6 anterior wall—Left main coronary
      - V1-2 reciprocal changes—Posterior wall, proximal RCA
    - Determine the type of ECG change
      - ST-segment depression—UA or NSTEMI (or "reciprocal" change of infarction in another location)
      - ST-segment elevation—STEMI or spasm (Prinzmetal's angina)
  - In an inferior wall MI (proximal RCA obstruction), check for a right ventricular infarction
    - An ECG with reversed V leads (right-sided ECG) demonstrates ST-segment changes in the right-sided V3-4.
  - In ACS the number of leads in which ST segment and T wave abnormalities are noted correlates with increased cardiac risk

- Sinus bradycardia, Wenckebach (Mobitz I) second-degree atrioventricular (AV) block, slow ventricular tachycardia (ventricular rate <100 bpm) suggests RCA involvement.
- Sustained rapid junctional tachycardia or Mobitz II second-degree AV block suggests left anterior descending (LAD) coronary artery involvement.

- Underlying conditions that interfere with the ECG diagnosis of ACS by obscuring the typical ST and T wave changes are:
  - Left bundle branch block (LBBB), ventricular pacemaker rhythm, preexcitation syndrome, myopericarditis, left ventricular hypertrophy with strain pattern and marked hyperkalemia

- Chest x-ray—portable technique
  - Chest x-ray is often totally normal with ACS.
  - May help exclude other causes for chest pain (pneumothorax, pulmonary embolus, aortic dissection, and pneumonia)
  - Cardiomegaly and heart failure point to intrinsic heart disease and increase the pretest likelihood of CAD.
- Cardiac biomarkers
  - Troponin T or I is a marker of choice.
    - Troponin elevates in 6 to 8 hours and may remain elevated up to 10 days.
    - Troponin T and I are equally sensitive and specific (90% sensitive and 95% specific), and both have enhanced prognostic value compared with creatinine kinase-MB fraction (CK-MB).
    - Serial troponin levels every 4 to 6 hours increase diagnostic capability for MI
    - Troponin levels are abnormal in STEMI and NSTEMI.
      - The World Health Organization's criterion for MI is a troponin level more than 99th percentile of normal (usually ≥0.6 ng/mL).
      - Troponins remain normal in UA (<0.6 ng/mL).
    - Normal troponin levels obtained less than 6 to 8 hours after the onset of pain cannot exclude acute myocardial damage.
    - Normal troponin levels obtained after 6 to 8 hours from the onset of pain may exclude MI but not unstable angina.
      - Of note, cell death often does not correspond with the onset of chest pain.
    - A single normal troponin level in a patient with suspected ACS should not generally be used as reassurance that discharge is safe.
    - The peak troponin elevation is directly related to the amount of myocardial damage.
  - CK-MB elevates in 6 hours but usually returns to normal within 3 days.
  - CK-MB is a better marker than troponins to diagnose reinfarction, if recurrent ischemic chest pain occurs post MI.
  - Troponin and CK-MB elevation may be noted in nonischemic cardiac disease (myopericarditis, cardiac contusion) and in noncardiac conditions (hypothyroidism, pulmonary embolus, sepsis, and renal failure on dialysis).

- Routine laboratory workup
  - Obtain a CBC, basic metabolic panel, and renal and liver panels.
  - Check for risk factors with a fasting lipid panel and fasting glucose levels.
  - Recommend checking resting oximetry and consider a TSH level.

RISK STRATIFICATION

- Echocardiogram
  - If ECG is nondiagnostic, and the patient is particularly ill, a transthoracic echo may demonstrate new segmental LV contraction abnormalities suggestive of ischemic heart disease.
  - Can help exclude other cardiac causes of chest pain (aortic stenosis, hypertrophic cardiomyopathy, or aortic dissection)
- Noninvasive stress or myocardial perfusion testing
  - Exercise treadmill or echocardiogram and pharmacologically assisted testing (adenosine/persantine, or dobutamine) is contraindicated in high-risk UA, acute NSTEMI, or STEMI.
- American College of Cardiology/American Heart Association (ACC/AHA) high-risk ACS criteria
  - New or presumed new ST-segment elevation
  - New or presumed new ST-segment depression
  - Recurrent ischemia despite intensive therapy
  - Recurrent ischemia with heart failure
  - Sustained ventricular tachycardia
  - Hemodynamic instability
  - Decreased systolic function
  - Elevated troponin level (>0.1 ng/mL)
  - High-risk finding on noninvasive stress or myocardial perfusion test
  - History of percutaneous coronary intervention (PCI) within 6 months
  - History of prior coronary artery bypass surgery

MEDICAL THERAPY

- Aspirin (ASA) 160 to 325 mg chewed stat; give additional dose even if on daily ASA, clopidogrel, or warfarin. Hold only if ASA allergy exists
  - Indicated for UA, NSTEMI, or STEMI
  - Continue at 75 to 81 mg PO daily
  - Decreases mortality after acute MI for at least 4 years
  - Decreases the risk of recurrent MI
  - Reduces incidence of nonfatal stroke after an MI

- Clopidogrel (Plavix) 300-mg loading dose then 75 mg PO daily
  - Use if ASA allergy
  - Consider with cardiologist/surgeon when a coronary artery bypass graft (CABG) will occur as clopidogrel may be held prior to an operation to prevent perioperative bleeding.
  - Use with ASA in high-risk UA, NSTEMI, STEMI and continue up to 12 months
  - Use post PCI with stent placement.
    - Continue for 1 month if bare metal stent used and *no* associated MI.
    - Continue for at least 3 to 6 months if drug eluting stent (DES) used and *no* associated MI. Because of recent concerns about late-onset thrombosis in DES, consider indefinite use of combined ASA plus clopidogrel until issue fully clarified.
  - Stop 5 to 7 days before elective surgery (CABG).
  - Monitor CBC for infrequent occurrence of TTP or neutropenia.
  - Reduces composite outcome of cardiovascular death, nonfatal MI, and stroke after acute MI
- Glycoprotein IIb/IIIa agents
  - Indicated for high-risk UA, NSTEMI with persistent or recurrent ischemia and urgent invasive therapy not readily available
    - Use eptifibatide or tirofiban
  - Used as adjunctive therapy with invasive PCI therapy
    - Use abciximab after PCI
  - Reduces death and nonfatal MI in high-risk ACS patients
- Nitrates
  - Sublingual (0.4 mg every 5 minutes times three doses), transcutaneous paste 0.5 to 2 inches every 6 hours, transcutaneous patch 0.2 to 4 mg/hr patch/day; IV start with bolus 12.5 to 25 μg, then drip of 5 to 10 μg/min; increase by 5 to 10 μg/min every 5 minutes (range 5 to 200 μg/min); oral isosorbide 20 to 40 mg every 12 hours
  - Used for symptomatic control of angina
  - If a phosphodiesterase-5 inhibitor (commonly used for erectile dysfunction) has been used in the last 24 hours (sildenafil, vardenafil) or 36 hours (tadalafil), nitroglycerin is contraindicated.
  - Caution with nitroglycerin use in older adults, in patients with diastolic dysfunction, or with a right ventricular infarction because these conditions are very volume-dependent states
- Morphine
  - Pain and anxiety relief
  - Dosage 2 to 5 mg IV and may be repeated under careful observation. Watch for hypotension.
- Unfractionated heparin (UFH) and LMWH
  - Frequently used for high-risk UA, NSTEMI, and STEMI
  - UFH may reduce in-hospital mortality in acute MI
  - LMWH (enoxaparin) appears to have a lower risk of recurrent MI, UA, need for revascularization, and heparin-induced thrombocytopenia.

- Enoxaparin should be dose adjusted with moderate renal impairment and withheld with advanced renal disease or if urgent surgery is contemplated.

- Beta-blockers
  - Metoprolol 5 mg IV every 2 to 5 minutes for three doses if chest pain is ongoing and heart rate tolerates, then continue maintenance dosage 25 to 50 mg PO every 6 hours. Oral metoprolol should be started if chest pain has resolved.
  - Acutely, beta-blockers relieve chest pain and reduce infarct size and risk of sudden death.
  - Post MI, beta-blockers reduce risk of reinfarction and mortality.
  - Attempt to titrate beta-blockers to achieve a resting heart rate of 55 to 65 bpm
  - Avoid in decompensated HF, heart block, hypotension, severe bronchospasm, or sinus node disease.
  - May mask signs of hypoglycemia
- Calcium channel blockers (CCBs)
  - If beta-blockers are contraindicated, consider use for rhythm control or recurrent ischemia.
  - Indicated for coronary spasm (Prinzmetal's angina)
  - Long-acting diltiazem and verapamil are the drugs of choice.
  - Avoid nifedipine post MI.
  - No mortality benefit (and possible adverse outcome) noted with CCB therapy
- Thrombolysis
  - Only indicated for STEMI within 12 hours of symptom onset when access to the coronary catheterization lab will be delayed
    - ST-segment elevation greater than 0.1 mV in contiguous leads or new LBBB with ischemic chest pain
  - Alternative therapy to early invasive therapy with PCI if PCI is not available
  - Fibrin-specific agents—Reteplase, alteplase, tenecteplase
  - Non-fibrin specific—Streptokinase
  - Reduces mortality in STEMI
    - Benefit greater in anterior wall versus inferior wall STEMI
    - Benefit greater with earlier therapy
  - Restores normal (thrombolysis in myocardial infarction [TIMI] 3) blood flow in 60% of patients
  - Increases risk of intracranial hemorrhage by 1.5% to 3% +
- ACE inhibitors
  - Indicated for high-risk UA, NSTEMI or STEMI patients
  - Starting oral doses: Ramipril (2.5 mg bid), captopril (6.25 mg tid), enalapril (2.5 mg bid) and lisinopril (5 mg daily)
  - Usually started 24 hours after an MI, but may be started earlier if persistent hypertension (HTN) despite therapy with beta-blockers and nitrates
  - Major benefit if LV systolic dysfunction, clinical heart failure (HF) and in patients with diabetes mellitus
    - Reduces mortality post MI at 24 months
    - In patients with LV dysfunction post MI, reduces rate of death, recurrent nonfatal MI, and hospitalization for HF

- Long-term protective effect in high-risk patients with CAD by reduction in death, MI, and stroke even without systolic dysfunction or HF
- Angiotensin II receptor antagonists
  - Alternative agents if ACE inhibitors cannot be used
  - Suggest starting losartan 25 mg PO daily or valsartan 80 mg PO twice daily
- Aldosterone blockers—Selective
  - Indicated post MI in patients with either LV systolic dysfunction or clinical HF
  - Eplerenone 25 to 50 mg PO daily started day 3 post MI
  - Watch for hyperkalemia.
    - Use agent with caution if creatinine clearance less than 50 mL/min
  - Reduces mortality and morbidity if used in patients post MI
- Warfarin
  - Indicated for ACS with atrial fibrillation, DVT, or endocardial thrombus
  - Reduces long-term mortality and venous and arterial thromboembolism
- HMG-CoA reductase inhibitors (statins)
  - Statins reduce cardiovascular death and provide primary and secondary prevention for stroke and MI.
  - Recommend early, aggressive statin therapy for their pleiotropic benefit
    - Atorvastatin 80 mg PO daily is the only proven agent for acute ACS treatment.
    - Evidence suggests that early aggressive statin therapy in ACS reduces symptomatic ischemia and recurrent hospitalizations.
  - Statins cause plaque stabilization, improve endothelial function, increase spontaneous thrombolysis and fibrinolysis, lower low-density lipoprotein (LDL) cholesterol, and decrease inflammation.
  - Cholesterol lowering begins within 2 weeks with maximal benefit at 6 weeks.

EARLY INVASIVE PERCUTANEOUS CORONARY INTERVENTION

- PCI is the preferred alternative to thrombolysis in high-risk UA, high-risk NSTEMI, and all STEMI and patients with cardiogenic shock.
- Goal is rapid primary PCI performed within 90 minutes of presentation to medical attention at a site with proven expertise (large volume centers with low mortality and morbidity).
- Hospital-to-hospital transfer for primary PCI is beneficial if procedure is performed within 2 hours of presentation.
- PCI after failed thrombolysis (salvage PCI) should be considered if persistent chest pain is present.

- Restores normal (TIMI 3) coronary blood flow in more than 90% of patients
- PCI reduces death, reinfarction, and stroke rate in ACS.

EARLY CORONARY BYPASS SURGERY (CABG)

- UA, NSTEMI, and STEMI patients with persistent or recurrent ischemia with unsuitable coronary anatomy for PCI
- Consider in patients with a critical left main coronary stenosis
- More frequently considered as a delayed form of complete revascularization in diabetic patients with multivessel disease, or in patients who otherwise require heart surgery (e.g., severe valve disease or rupture of mitral valve or intraventricular septum)

ACUTE PERICARDITIS

Acute pericarditis involves the acute inflammation of the pericardial sac. Ninety percent of cases are either of idiopathic or viral etiology. Most cases of acute pericarditis are self-limited, but recurrent pericarditis develops in 15% to 32% of cases. Other causes of pericarditis include neoplasm, infections (tuberculous [Tb], bacterial, fungal, rickettsial or parasitic), sarcoidosis, Dressler's syndrome (post MI), post irradiation, chest trauma, uremia, hypothyroidism, post pericardiotomy, connective tissue diseases (systemic lupus erythematosus, scleroderma, and RA) and medications (hydralazine, methyldopa, isoniazid, phenytoin, and procainamide).

Symptoms

- Constant, sharp, or stabbing retrosternal chest pain
- Exacerbating factors: Deep inspiration and lying down, +/- with swallowing
- Alleviating factors: Improved with leaning forward
- Radiation pattern: Neck, shoulders, arms, trapezius ridges, or epigastrium
- Malaise, myalgias, dry cough, and dyspnea are common.

Signs

- Pericardial rub heard ++++
- Harsh, high-pitched, scratchy sound best heard at end expiration, leaning forward
- Classic rub with three components best heard at the cardiac apex: Ventricular systole, early diastole, and atrial contraction
- Triphasic +++
- Biphasic and monophasic rubs ++
- Signs of cardiac tamponade: Hypotension, tachycardia, jugular venous distension and pulsus paradoxus (fall in systolic BP >10 mm Hg with inspiration) and muffled heart sounds if associated with a large pericardial effusion.
- Temperature greater than 38° C uncommon + except in purulent pericarditis

ELECTROCARDIOGRAPHIC CHANGES

- Stage 1: Diffuse, concave ST-segment elevations and diffuse PR segment depressions (mainly in leads I, II, aVL, aVF and V3-6); however, lead aVR will demonstrate ST-segment depression and PR segment elevation.
- Stage 2: ST and PR segments normalize and T waves progressively flatten.
- Stage 3: Diffuse T wave inversions
- Stage 4: Normalization of the T waves
- ECG changes can be seen. ++++
- No Q wave formation or loss of precordial R wave progression in acute pericarditis
- Electrical alternans may be seen if a large pericardial effusion exists.
- The ratio of ST-segment elevation (in millimeters) to T wave amplitude (in millimeters) greater than 0.24 in lead V6 is highly specific for acute pericarditis.
- Diffuse T wave inversions and concave ST elevation with PR depression suggests myopericarditis

INDICATIONS FOR HOSPITALIZATION

- Fever more than 38° C, subacute onset over weeks, immunocompromised, history of trauma, anticoagulant therapy, myocarditis, elevated troponin I, evidence of cardiac tamponade or a large pericardial effusion (echo-free space >2 cm)

Workup

- Routine labs: CBC, renal panel, ESR, and troponins
- Troponin I: Mild elevations in up to 70% of patients ++++ with pericarditis and marked elevations consistent with myopericarditis
- Potential labs: Antinuclear antibody, rheumatoid factor and a tuberculous skin test
- Pericardial fluid analysis: Glucose, protein, lactic dehydrogenase, cell count, culture, and Gram stain. If Tb or neoplasm is suspected, send fluid for cytology, *Mycobacterium tuberculosis* ribonucleic acid (RNA) by PCR assay and adenosine deaminase activity (>30 units/L suggests Tb pericarditis)
- Chest radiograph
- Echocardiogram indications: All patients with acute pericarditis should have a transthoracic echocardiogram. This is especially important for prolonged symptoms, any evidence of cardiac

tamponade, or any suspicion of purulent or neoplastic pericarditis or myocardial involvement.
- Global or regional wall motion abnormalities suggest myopericarditis.

Treatment
- Treatment of symptomatic pericarditis related to viral, idiopathic, autoimmune, or connective tissue etiologies
- Oral indomethacin 75 to 225 mg/day or ibuprofen 1600 to 3200 mg/day
- Oral colchicine 1 to 2 mg/day on day 1 then 0.5 to 1 mg/day for 6 months can be added if symptoms persist for more than 2 weeks or for recurrent pericarditis.
- Prednisone 1 to 1.5 mg/kg/day orally for at least 1 month then taper over several months if severe, recurrent pericarditis or if connective tissue disease etiology.
- Idiopathic and viral pericarditis will spontaneously resolve in 2 to 6 weeks.
- Acute pericarditis from bacterial, Tb or neoplastic causes requires treatment of underlying condition and often requires creation of a pericardial window.
- Most common bacteria found in purulent pericarditis are *Staphylococcus, Streptococcus,* and *Haemophilus.* Empiric antibiotics typically include an antistaphylococcal antibiotic and an aminoglycoside antibiotic. Obtain an early cardiothoracic surgery consultation.
- Start isoniazid, ethambutol, rifampin, and pyrazinamide for Tb pericarditis.
- Pericardiectomy is indicated only in highly symptomatic, recurrent pericarditis refractory to medical management.
- Indications for pericardiocentesis: Therapeutic for clinical evidence of tamponade or diagnostic for possible purulent, Tb, or neoplastic pericarditis

AORTIC DISSECTION

No chest pain diagnosis is more dependent on the evaluator's index of suspicion than thoracic aortic dissection. Studies show that physicians correctly suspect aortic dissection in as few as 15% to 43% of patients on initial presentation—in a condition with a 48-hour mortality rate approaching 40% to 68% in untreated patients. Failure to correctly and expediently diagnose aortic dissection may lead to disastrous results, particularly if anticoagulation and/or thrombolysis is used for presumed cardiac ischemia.

Symptoms
- Sudden onset, severe, "tearing" chest pain radiating to the back, neck, or abdomen caused by the extension of a tear between the

intima and adventitia layers of the thoracic aorta, thereby creating a "false lumen" in the arterial wall ++++
- Often has a migrating quality to the chest pain +++
- May present as syncope or sudden collapse ++

Signs
- Reduced or asymmetric pulses (carotid, femoral, and radial) or blood pressures +++
- Diastolic murmur (aortic regurgitation from extension to the aortic valve) with radiation to the right or left sternal border +++
- Neurologic deficits such as stroke or paraplegia from carotid or spinal artery involvement ++
- Acute limb ischemia (look for the six "P's") ++
  - Affected limb with pain, pallor, paralysis, paresthesia, pulseless, poikilothermia
- Acute inferior wall MI (right coronary artery occlusion) +
- Cardiogenic shock from dissection into the pericardium causing tamponade ++
- Acute renal failure by involvement of the renal arteries (decreased urine output) ++

Workup
- Chest x-ray often shows a widened mediastinum (44% to 80%) or abnormal aortic contour (56% to 84%).
- Chest CT with IV contrast (preferably helical), transesophageal echocardiogram (TEE), or MRI of the chest with gadolinium
- ECG, cardiac enzymes, and D-dimer are all nonspecific.

Comments and Treatment Considerations
Risk factors include age greater than 50 years; hypertension; coarctation of the aorta; bicuspid aortic valve; trauma; Marfan, Ehlers-Danlos, and Turner syndromes; giant-cell arteritis; syphilitic aortitis; third-trimester pregnancy; family history of aortic dissection or rupture; cocaine abuse; intra-aortic catheterization; and history of cardiac surgery.

Classification systems for aortic dissection include Stanford classification and Debakey classification. Stanford classification has two kinds of classifications. Type A involves ascending aorta, regardless of the site of origin. Type B involves descending aorta with origin distal to the left subclavian artery.

Debakey classification has four types. Type I involves ascending the aorta, aortic arch, and possibly descending aorta. Type II involves the ascending aorta only. Type III A involves the descending aorta only, with proximal and distal extension. Type III B involves the descending aorta with distal extension into abdominal aorta.

Patients need excellent blood pressure and heart rate control in acute aortic dissection. Using labetalol IV to keep systolic blood pressure less than or equal to120 mm Hg is first-line

therapy. Alternative agents include IV nitroprusside, esmolol, or diltiazem.

Ascending aorta dissections usually require urgent surgical repair and management. Descending aorta dissections may be medically managed.

CHRONIC STABLE ANGINA

In the medical office of a primary care physician, the majority of chest pain is noncardiac in origin (90%), +++++ whereas in the ER the likelihood may exceed 50%. +++ The probability that CAD is present is based on the characterization of the patient's chest pain, gender (men > female,) and advancing age.

 CLASSIC ANGINA

Symptoms

- Typically, chest pressure or squeezing sensation
- Pain radiates to the shoulders, neck, jaw, epigastrium or left arm
- Pain similar to prior angina or MI
- Pain associated with nausea, vomiting, or diaphoresis
- Precipitated by physical (upper > lower extremity) or emotional stress
- Lasts up to 15 minutes
- Resolves with rest or nitrate therapy within 5 to 15 minutes
- May resolve more slowly if related to emotional stress
- Stable angina is chest pain with a reproducible onset after a predictable level of exertion or stress and of a predictable duration.

 ATYPICAL ANGINA

- One or at most two of the above classic characteristics
- Pain localized to a small discrete area of the chest wall
- Pain starting at maximal intensity, or constant pain lasting for hours to days
- Atypical pain is more commonly noted in women, older adult patients, diabetic patients, and patients with renal disease.
- May present as dyspnea, sudden fatigue, or nausea

 TRADITIONAL CHARACTERIZATION OF "NONCARDIAC PAIN"

- Up to 25% of MIs may be "silent," so clinical criteria are not completely reliable.
- None or at most one of the classic characteristics ++++
- Pain that is not exacerbated by effort ++++

- Pain lasting only seconds ++++
- Pain exacerbated with swallowing, deep breathing, coughing, palpation, or position changes ++++

VARIANT ANGINA

- Has typical angina characteristics but occurs only at rest
- It is not initiated by physical effort

Signs

- Not common with stable angina
- Are related to sudden decrease in systolic or diastolic LV function
- Transient hypotension during chest pain +
- Transient cardiac gallops (S_3 or S_4) during chest pain +
- Transient mitral insufficiency (papillary muscle dysfunction) during pain +

ELECTROCARDIOGRAM

Workup

- May be normal in 50% of patients with CAD, even if obtained during pain
- Location: ECG leads related to coronary anatomy
  - II, III, aVF—Inferior wall, RCA
  - V1-V3—Anteroseptal wall, left anterior descending coronary
  - I, aVL, V4-6—Anterolateral wall, circumflex coronary
  - I, aVL, V1-6—Anterior wall, left main coronary
  - V1-2 reciprocal changes—True posterior wall, proximal RCA
- Type of ECG change
  - ST-segment depression—Cardiac ischemia (typical angina)
  - ST-segment elevation—Cardiac injury or spasm (Prinzmetal's angina)
- Treadmill
  - Can diagnose angina and risk-stratify patient
  - The severity of the pain does not correlate with the quantity of myocardium at risk.
  - If baseline ECG is normal or only mildly abnormal (<1 mm ST depression or right bundle branch block [RBBB]), and patient can exercise, order routine treadmill (sensitivity 68%/specificity 77%).
  - If baseline ECG is abnormal, and patient can exercise, order exercise echocardiogram (sensitivity 76%/specificity 88%) or exercise myocardial perfusion imaging (MPI) study (sensitivity 88%/specificity 77%).

- If patient cannot exercise, adenosine/persantine (sensitivity 90%/specificity 75%) or dobutamine MPI (sensitivity 82%/specificity 75%)
  - Thallium isotope if weight less than 250 pounds and Cardiolite if more than 250 pounds
- Consider using Duke Treadmill Score for risk stratification.

ECHOCARDIOGRAM

- CAD is associated with segmental LV contraction abnormalities.
- Can help exclude other cardiac causes of chest pain (aortic stenosis, hypertrophic cardiomyopathy, mitral valve prolapse, or aortic dissection)

ROUTINE LABORATORY WORKUP

- Obtain a CBC, basic metabolic panel, renal, liver panels, and a TSH level.
- Check for risk factors with a fasting lipid panel and fasting glucose levels.

MEDICAL THERAPY

- Reduces symptoms, prevents myocardial infarction, and improves survival
- Nitrates (sublingual, spray, oral, or transdermal)
  - Reduces symptoms by decreasing cardiac preload and by coronary dilation
  - Sublingual tablet or spray every 5 minutes for three doses or until pain resolves
  - Long-acting nitrates as effective as long-acting CCBs and cause less BP lowering
  - Can be used with either beta-blocker or CCB
  - Need a 14-hour nitrate-free interval to prevent drug tolerance

ASPIRIN

- Dosage: 75 to 325 mg PO daily
- Recommended in acute or chronic disease with or without symptoms

Clopidogrel

- 300-mg loading dose then 75 mg PO daily
- Use if ASA allergy

- Should stop 5 to 7 days before elective major surgery (e.g., CABG) (use with caution if going to catheterization for STEMI and possibility of early CABG)
- Monitor CBC for rare occurrences of TTP or neutropenia.
- Less GI bleeding and GI upset compared with ASA

BETA-BLOCKERS

- Improve survival in patients with prior MI
- Reduce symptoms by decreasing cardiac demand
- Titrate beta-blockers to achieve a resting heart rate 55 to 65 bpm.
- Avoid in patients with sinus or AV nodal disease, severe reactive airway disease, or decompensated heart failure.

CALCIUM CHANNEL BLOCKERS

- Improve symptoms by coronary dilation, and by decreasing cardiac demand and systemic afterload
- Long-acting CCBs are indicated when beta-blockers are contraindicated, not effective, or cause unacceptable side effects.
- They relieve angina, increase exercise time to ischemia, and decrease the need for sublingual nitrates.
- They should be combined with beta-blockers or long-acting nitrates whenever possible.
- Long-acting CCBs offer no mortality benefit and possibly confer an increased risk of cardiovascular events when used as a solo agent.
- Short-acting CCBs should be avoided due to increased risk of adverse cardiac events.
- Long-acting non-dihydropyridine CCBs (diltiazem, verapamil) decrease angina, slow sinus and AV nodal function, and are negatively inotropic
  - Avoid use with beta-blockers.
  - Use with long-acting nitrates is beneficial.
- Long-acting dihydropyridine CCBs decrease angina by coronary dilation and by decreasing afterload
  - May be used with beta-blockers
  - Use with long-acting nitrates may cause excessive hypotension.

ACE INHIBITORS

- Not indicated for angina relief
- Improve survival if CAD is associated with LV dysfunction, diabetes mellitus, HTN, or prior MI

- Beneficial with chronic proteinuria by delaying progression of renal disease
- May be beneficial in all high-risk patients with CAD (HOPE trial)

INVASIVE THERAPY

- PCI indications
  - High-risk angina
  - High-risk treadmill (large area of ischemia or ischemia at low workload)
  - Resistant angina despite optimal medical therapy
  - Two- or three-vessel CAD in nondiabetic patients
- Coronary artery bypass surgery (CABG)
  - Improves survival with left main coronary disease, triple vessel disease with decreased ejection fraction, double vessel disease with proximal left anterior descending artery stenosis
  - Significant coronary artery disease associated with need for open heart surgery for other reasons
  - Significant coronary artery disease not amenable to PCI
  - Symptomatic angina with triple vessel disease in diabetic patients

Comments and Treatment Considerations

Angina pectoris is a symptom of imbalance between oxygen *supply* via the coronary arteries and cardiac *demand* based on elevated heart rate, blood pressure, contractility, or wall stress (related to ventricular volume and mass). This imbalance occurs most commonly by decreasing supply due to plaque formation (≥70% obstruction), plaque rupture, or ulceration. Decreased supply may also be due to hypotension, coronary spasm, or embolism.

Increasing cardiac demand may be related to sustained systemic hypertension, increased physical activity, emotional stress, or the presence of cardiac hypertrophy or cardiac enlargement. Because coronary perfusion occurs predominantly during diastole, prolonged tachycardia adversely affects both cardiac supply and demand.

Risk factors for stable angina are identical to those for ACS.

GERD-RELATED CHEST PAIN

See Chapter 26.

HERPES ZOSTER

Included in every differential diagnosis of chest pain should be a consideration of herpes zoster infection or "shingles." Most clinicians assume that a diagnosis of herpes zoster would be self-evident by a simple visual inspection of a patient's chest and trunk. Classically, herpes zoster reactivation manifests as a painful, itchy,

erythematous vesicular eruption that follows a unilateral dermatome. However, the key is that pain with shingles may precede any semblance of rash by several days.

Varicella-zoster virus, which causes chickenpox, remains in a dormant stage in the dorsal root ganglia. On reactivation the virus travels through the sensory nerve fibers, manifesting as a rash in specific dermatomal distributions. Zoster is most commonly seen in older adults and in chronically immunosuppressed patients, particularly HIV/acquired immunodeficiency syndrome (AIDS) patients, and those receiving chemotherapy, corticosteroids, and other immunosuppressive medications.

Symptoms

- Prodrome of headache, ++ malaise, ++ dysesthesias, ++ and rarely fever +
- Pain of variable severity and typically "burning" in quality ++++
- History of chickenpox +++++

Signs

- Erythematous, pruritic, painful eruption with fluid-filled vesicles that follow a specific dermatome and does not cross midline ++++
- Vesicles and rash usually evolve over days to form ulcerations and crust.
- Resolution phase occurs over weeks and may be complicated by scarring, variation in pigmentation, and postherpetic neuralgia (PHN).
- Contiguous dermatomes may be involved in 20% of cases, but are nonadjacent. ++
- Bilateral dermatomal involvement is exceedingly rare except in immunocompromised patients in whom disseminated zoster can occur. +
- Thoracic and lumbar dermatomes are involved most commonly. ++++

Workup

- Herpes zoster is usually a clinical diagnosis based on historical and physical examination findings.
- If the presentation is atypical, particularly in immunocompromised patients, there are several methods to confirm the diagnosis:
  - Viral cultures of vesicular fluid for herpes zoster
    - Long turn-around time and false-negative results are common if inadequate specimen obtained
  - Tzanck smear
    - Floor of the vesicle scraped onto slide and then stained with Wright's or Giemsa stain
    - Will have result fast, but does not distinguish from herpes simplex infection
  - Direct antigen staining
    - Similar to Tzanck smear except material on slide sent to laboratory for direct antigen staining for herpes zoster antigen

- Advantages include quick turn-around time and test is highly sensitive and specific.
- In otherwise healthy, young patients without apparent risk factors for zoster, consider checking HIV status.
- In patients with evidence of involvement of the first branch of the trigeminal nerve (vesicles on the forehead, tip or side of the nose, swelling of the eyelid, or conjunctivitis) consider emergent consultation with ophthalmologist because of the risk of herpes zoster ophthalmicus, which may threaten vision.
- Patients with involvement of the pinna or external auditory canal may develop facial nerve palsy, often with ipsilateral hearing impairment (Ramsay-Hunt syndrome).

Comments and Treatment Considerations

The goals of treatment are to reduce symptoms of zoster and to prevent complications. Zoster is usually a self-limited illness in immunocompetent patients. The main complication in these patients is the development of PHN, which is defined as pain that persists beyond 30 days from the onset of rash and may last up to months or years. There is a direct correlation between a patient's age and duration of PHN.

In immunosuppressed patients, diligent observation must be undertaken for the development of disseminated zoster infection.

The mainstay of treatment for zoster are antiviral medications. Initiate antivirals if rash started in the last 72 hours and treat for 7 to 10 days with acyclovir (800 mg five times a day), valacyclovir (1000 mg every 8 hours), and famciclovir (500 mg every 8 hours). Studies have shown benefit compared with placebo administration in halting new lesion formation, shortening the duration of viral shedding and zoster-associated pain, but no conclusive evidence for the prevention of PHN. Antivirals are more beneficial the sooner they are started after symptom onset. Adjust antiviral dosages in patients with renal impairment.

Adjunctive corticosteroids therapy: Evidence suggests that steroids lead to an acceleration in cutaneous healing and an earlier resolution of acute pain. Steroid therapy has no clear effect on PHN. Symptomatic treatment may include narcotics when pain is not relieved with oral analgesics. Care should also be taken to keep lesions clean and dry to prevent bacterial superinfection.

Patients infected with zoster remain infectious up to the point when the last lesion crusts over. Care should be taken for contagious patients to avoid contact with anyone who does not have a history of varicella infection; the most vulnerable individuals are pregnant women and immunocompromised hosts. Zostavax is a new vaccine that has been FDA approved for the prevention of herpes zoster in persons 60 years and older who have a history of chickenpox.

MUSCULOSKELETAL CHEST WALL PAIN

Musculoskeletal chest wall pain is the established cause of chest pain in up to one third of cases seen in an outpatient setting. +++ It also must be entertained as a diagnosis in the ER despite the lower

prevalence there (approximately 7%). ++ It is difficult to make this diagnosis within the ER because a sizable percentage of patients who ultimately are shown to have chest pain of cardiac etiology will have "reproducibility" of pain through palpation or movement. Establishing a musculoskeletal cause of chest pain can not only alleviate anxiety around the concern of a life-threatening cause of pain, but also obviate the need for expensive testing.

A diverse array of anatomic structures in and around the thorax (e.g., muscles, fascia, bone, cartilage, and nerves) may be responsible for musculoskeletal chest pain. Chest pain of musculoskeletal origin is a diagnosis of exclusion; more serious disorders involving the cardiovascular, pulmonary, and gastrointestinal systems must be excluded.

Symptoms

- Pain is often localized, nagging, and insidious in onset.
- Pain may be acute, stabbing, and often radiates to other locations.
- Pain is often exacerbated by movement.
- Pain is usually relieved by analgesics and local application of heat.

Signs

- Biceps tendinitis, pectoral myofasciitis, intercostal muscle spasm, or inflammation
  - Localized pain at the respective anatomic site worsened by direct palpation or movement of those muscle groups ++++
- Costochondritis
  - Tenderness at the costochondral junction ++++
  - "Tietze's syndrome" if localized swelling also present
- Sternoclavicular arthritis, manubriosternal arthritis, xiphoid process pain
  - Localized tenderness at these articulations ++++
  - Often present with systemic arthritides
- Cervical or thoracic spine arthritis or disk disease
  - Tenderness often elicited on spinous process palpation +++
  - Dermatomal distribution of pain is elicited by careful examination of the chest wall.
  - High index of suspicion is needed if pain is the only symptom
  - Distal neurologic findings may be found with progression of the lesion.
- Rib or intercostal muscle trauma
  - Tenderness at the site of trauma ++++
  - Often exacerbated by truncal movement and breathing +++
- Bony pain from metastases
  - Palpable tender mass may be appreciated at the site of metastasis.
- Shoulder pain
  - Provocative testing of passive and active ROM of the shoulders will elicit pain with radiation to the chest wall.

- Fibromyalgia
  - Tenderness elicited at 11 or more of a possible 18 tender points ++++
  - Trigger point image available at www.triggerpoints.net

Workup

- ECG is generally indicated even if suspicion of musculoskeletal etiology is high.
- Chest radiography may be indicated to rule out pneumothorax, pneumonia, or rib fractures among other etiologies.

Comments and Treatment Considerations

Replication of the patient's chest pain by palpation of the chest wall is 87% specific for the diagnosis of musculoskeletal chest wall pain. Nevertheless, 7% of chest pain reproduced by palpation may be associated with cardiac ischemia or pulmonary emboli.

Musculoskeletal chest pain may occur in isolation, or may be present concurrently with other causes of chest pain. Analgesics, including acetaminophen, NSAIDs, and/or opiate analgesics along with local measures such as heat application may be indicated for symptomatic relief of musculoskeletal chest pain. Physical therapy may be beneficial for musculoskeletal chest pain unresponsive to these measures. Complete resolution of the chest pain after local injection of lidocaine into the affected region can both diagnose musculoskeletal chest pain and provide therapeutic relief.

PNEUMONIA

See Chapter 16.

PNEUMOTHORAX

See Chapter 38.

PULMONARY EMBOLUS

Approximately 600,000 cases of pulmonary embolus (PE) are diagnosed in the United States annually. PE accounts for 10% of all hospital deaths, and the attributable mortality from a PE is 15% to 30%. Making a firm diagnosis of a PE can be challenging because the diagnosis of a PE must take into account the clinical pretest probability (by the modified Wells clinical prediction tool [Fig. 12-1]), results of a high sensitivity D-dimer test, and results of noninvasive imaging studies. The clinical pretest probability for a PE is a critical determinant for the interpretation of noninvasive imaging studies during a PE workup.

PE falls under three different classifications: uncomplicated, submassive, and massive. An uncomplicated PE has no hemodynamic

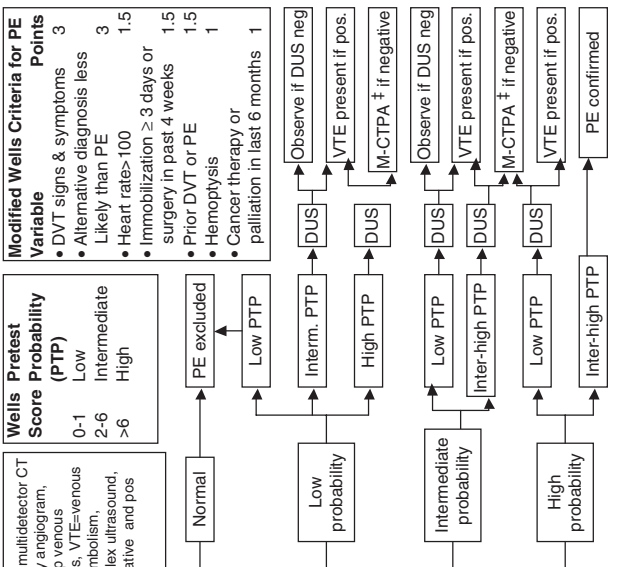

FIGURE 12–1 Diagnosis of pulmonary embolus.

compromise or ventilatory dysfunction. A submassive PE causes secondary pulmonary hypertension and right heart strain, but there are no signs of shock. A massive PE is usually the result of a "saddle embolus," which obstructs blood flow to the pulmonary arteries causing obstructive shock.

Symptoms

- Dyspnea ++++
- Pleuritic chest pain +++
- Cough +++
- Leg pain ++
- Hemoptysis ++
- Palpitations ++

Signs

- Tachypnea: Respiratory rate greater than 20 ++++
- Rales +++
- Leg swelling +++
- Tachycardia: Heart rate more than 100 bpm +++
- Wheezes ++
- Diaphoresis ++
- Fever: Temperature more than or equal to 38.5° C ++
- Pleural rub +

Workup

- Investigate for any risk factors for a venous thromboembolism (VTE).
- All patients should have a thorough history and examination because 10% to 20% of patients with an idiopathic VTE have an underlying malignancy.
- Investigate for any family history of clotting problems or cancer.
- The chest radiograph may be normal or show either atelectasis or a pleural-based density.
- An ECG typically shows only sinus tachycardia.
- In one third of patients with a submassive or massive PE, the ECG shows signs of acute right heart strain, often with an S1Q3T3 pattern.
- CBC, BMP, and high-sensitivity D-dimer test
- Recommend using a quantitative, rapid ELISA D-dimer test (sensitivity 95%)
- Pulse oximetry is usually adequate.
- An arterial blood gas is generally not helpful in making the diagnosis of PE because there is a normal alveolar-arterial oxygen gradient in up to 20% of patients with a PE. It can provide information about ventilation (assess $PaCO_2$).

RISK STRATIFICATION OF PE

Troponin I

- Troponin I is increased in 16% to 39% of patients with a documented acute PE.
- Troponin I is thought to be a surrogate marker for right ventricular dysfunction.
- The mortality rate approaches 33% when troponin I levels exceed 2 ng/mL.

Echocardiogram

- Right ventricular dysfunction/strain exists if any of the following are present:
  - RV diameter/LV diameter greater than 0.9
  - RV enlargement and loss of inspiratory collapse of the inferior vena cava
  - Evidence of marked pulmonary hypertension

NONINVASIVE IMAGING TESTS FOR PE

Ventilation-perfusion (V/Q) Scans

- Diagnostic algorithm using V/Q scans
- Most V/Q scans will be indeterminate (73% of scans in the original Prospective Investigation of Pulmonary Embolism Diagnosis [PIOPED] study).

MULTIDETECTOR CT PULMONARY ANGIOGRAMS (MCTPAS)

- The sensitivity of MCTPA alone is 83% and the specificity is 96%.
- In low-risk populations a negative MCTPA has a negative likelihood ratio of 0.07 and a negative predictive value (NPV) of 99.1% against having a significant venous thromboembolic event within 3 months. The predictive value of an MCTPA depends on the pretest probability as shown in Table 12-1. The NPV of a normal MCTPA is identical to that of a negative catheter pulmonary angiogram.
  - Additional benefits: MCTPAs can identify an alternative diagnosis two thirds of the time when a PE is not present; and the scan can assess for right ventricular enlargement, which can be a marker of right ventricular strain in a submassive PE.
  - MCTPA limitations: They are often not interpretable if there is motion artifact or in very obese patients with a body mass index (BMI) greater than 35; they have poor sensitivity for detecting subsegmental pulmonary emboli; and they require the administration of IV contrast.

Table 12-1. Predictive Value of Diagnostic Tests Based on Clinical Pretest Probability (PTP) in Patients with an Elevated D-Dimer Level

TESTING	LOW PTP	INTERMEDIATE PTP	HIGH PTP
MCTPA	NPV = 96% PPV = 58%	NPV = 89% PPV = 92%	NPV = 60% PPV = 96%
MCTPA-CTV	NPV = 97% PPV = 57%	NPV = 92% PPV = 90%	NPV = 82% PPV = 96%

MCTPA-CTV, Multidetector computed tomography pulmonary angiogram-computed tomography venogram; *NPV,* negative predictive value; *PPV,* positive predictive value.

Adapted from PIOPED II data in Stein PD, Woodard PK, Weg J, et al: Diagnostic pathways in acute pulmonary embolism, *Am J Med* 119:1048-1055, 2006.

DUPLEX ULTRASOUND OF LOWER EXTREMITIES

- A lower extremity duplex ultrasound is indicated when the V/Q scan results are indeterminate. In this case, a duplex ultrasound documenting a DVT obviates the need for an MCTPA.

CT VENOGRAM (CTV)

- Can be performed simultaneously with an MCTPA and increases sensitivity of VTE detection from 83% to 90%. Specificity is 95%.

A HYPERCOAGULABLE WORKUP

- Candidates for a hypercoagulable workup
  - High likelihood of a thrombophilia: Idiopathic PE less than 45; recurrent PE; first-degree relative with PE less than 50; cerebral or visceral vein thrombosis; any pregnancy-, postpartum- or estrogen-related VTE; or any history of a stillbirth or three or more unexplained spontaneous abortions in less than 10 weeks
- What to order: Check activated protein C (APC) resistance, prothrombin gene mutation, anticardiolipin antibody, lupus anticoagulant, and levels of plasma homocysteine, antithrombin III, protein C, factor VIII activity, and protein S
- When to order it: Check all lab tests after completing anticoagulation and the patient has been off of warfarin for at least 2 weeks.

DIAGNOSIS OR EXCLUSION OF PE (See Fig. 12-1)

- PE is excluded if:
  - A normal high-sensitivity D-dimer and a low pretest probability.
    - Normal high-sensitivity D-dimer and intermediate pretest probability exclude most cases of PE (NPV is 95%).
  - A normal MCTPA and low-intermediate pretest probability
  - Normal serial MCTPA and high pretest probability
  - Normal catheter pulmonary angiogram
  - A normal V/Q scan
  - A low-probability V/Q scan and a low clinical pretest probability
- Diagnosis of PE if:
  - PE visualized on an MCTPA
  - A high-probability V/Q scan and intermediate to high pretest probability

Comments and Treatment Considerations

The vast majority of patients with an acute PE will be treated in the hospital with acute heparinization and transitioned to long-term warfarin therapy. Exceptions include a submassive/massive PE for whom thrombolysis should be considered and those with a contraindication to anticoagulation who need placement of an inferior vena cava (IVC) filter. Patients with active cancer who have had an acute PE should receive LMWH for 3 to 6 months prior to transitioning to warfarin therapy.

In patients without absolute contraindications, start either heparin or LMWH and warfarin simultaneously and overlap at least 5 days and until international normalized ratio (INR) is greater than or equal to 2 for 24 hours. Give 80 units/kg IV bolus of heparin, then begin a drip at 18 units/kg/hr and titrate to maintain aPTT 1.5 times the upper limit of normal. LMWH: enoxaparin 1 mg/kg subcutaneously q12h or tinzaparin 175 units/kg subcutaneously daily. Warfarin: Typical starting dose is 5 mg PO daily in most adults.

Duration of anticoagulation:

- 3 months: DVT with transient risk factors
- 6 to 12 months: Idiopathic PE
- Until 6 weeks postpartum: PE during pregnancy
- Indefinite: Idiopathic life-threatening PE, PE with permanent thrombophilic state (e.g., cancer or high-risk hypercoagulable state)

THROMBOLYSIS

- The American College of Chest Physicians suggests that patients who are hemodynamically unstable from a massive PE are candidates for systemic thrombolysis with tPA 100 mg infused over 2 hours (grade 2B).
- Thrombolysis for submassive PE resulted in a decreased need for vasopressor use, but no statistically significant mortality benefit.
- IV tPA has a 2% to 3% risk of intracranial hemorrhage and a 0.5% risk of death.

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